REMARKS/ARGUMENTS

Claims 1, 3, and 4; and 18-33 are pending in the application.

Claims 2, 5-18, and 20 have been canceled without prejudice or waiver.

Claims 1, 3, 4, 18, 19, and 21-33 stand rejected.

Applicants' are filing with this response a new oath and declaration which now includes the priority application USSN 09/017,412 and Canadian priority application No. 2196496 as requested in the outstanding office action.

PRIORITY

Regarding the priority of the instant application (See pages 2 and 3 of the outstanding office action); Applicant has now complied with the filing of the new oath/declaration claiming priority to USSN 09/017,412 and Canada Application 2196496. Accordingly, the claimed subject matter of the instant application gets the priority of the above two priority documents.

It is also respectfully submitted that there is enough disclosure in the earlier parent case (09/017,412) to support in vivo screening. See in particular Example 7.

INTERVIEW OF JULY 15th , 2004 AND SUMMARY

Applicants' would like to thank Examiner Ponnaluri for the courteous interview conducted on July 15th 2004. During the interview the Examiner discussed the need for a new oath/declaration. This need has now been fulfilled by the filing a new declaration together with this amendment.

The pending claims were discussed and in view of the new priority claimed in the new declaration which now includes the Canadian priority CA 2196496 (filed January 31, 1997), it was concluded that all the prior art of record has been rendered moot or not-relevant as the priority date precedes the publication dates of the references of record.

THE REJECTION UNDER 35 U.S.C. § 112 FIRST PARAGRAPHS

The rejection of claims 1, 3-4, 18-19, 21-24 and 31-32 under 35 § USC 112 first paragraph is respectfully traversed. The Examiner asserts that the specification is only enabling for dihydrofolate reductase as the reporter molecule and the use of leucine zipper molecules as panel of molecules in the method of identifying an interacting set of molecules.

The Examiner asserts that "the specification does not enable any person skilled in the art to which it pertains, or with which it is mostly connected, to make and use the invention commensurate in scope with this claims". This assertion is respectfully traversed. In view that this application now claims CIP status from US serial No. 09/017,412 now US Patent No. 6,270,964 (see below), it is respectfully submitted that there is sufficient guidance in the earlier application as to the selection of a reporter molecule as well as sufficient Examples of the types of reporters that are desirable. Furthermore, the patent statute is also clear regarding enablement. As long as there is sufficient guidance from the specification, there is really no requirement for an example, however Applicant has provided Examples to illustrate the invention.

Furthermore, Applicants' parent case goes into exquisite detail regarding selection

of reporters and uses in screening. There is no undue experimentation if applicant follows the procedures outlined for reporter selection and uses in library screening.

It should be pointed out that the US Patent Office training manual (at 8) regarding 35 USC 112 first paragraph points out that:

"Before any analysis of enablement can occur, it is necessary for the Examiner to construe the claims. For terms that are not well known in the art, or for terms that could have more meaning, it is absolutely necessary that the Examiner select the definition that he/she intends to use when examining the application, based on his/her understanding of what applicant intends to mean, and explicitly set forth the meaning of the term and the scope of the claim when writing an office action"

The manual also emphasizes the precept that the absence of a working example, as such, does not necessarily compel a conclusion of nonenablement, even in the unpredictable arts.

The MPEP, Section 2164.02 states: "the specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation."

Additionally the manual states that "the presence of only one working example should never be the sole reason for making a scope rejection, even though it is a factor to be considered along with all the other factors. To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims."

Applicant also has shown in its prior US patent No. 6,270,964; how to select, enable and design a reporter molecule and what are the requirements for successfully performing a PCA using the multitude of reporters which have been exemplified. For the Examiners' benefit those design requirements are outlined below (See from col. 3 , line 58 to col. 4, line 42:

"One particular strategy for designing a protein complementation assay (PCA) is based on using the following characteristics: 1) A protein or enzyme that is relatively small and monomeric, 2) for which there is a large literature of structural and functional information, 3) for which simple assays exist for the reconstitution of the protein or activity of the enzyme, both in vivo and in vitro, and 4) for which overexpression in eukaryotic and prokaryotic cells has been demonstrated. If these criteria are met, the structure of the enzyme is used to decide the best position in the polypeptide chain to split the gene in two, based on the following criteria: 1) The fragments should result in subdomains of continuous polypeptide; that is, the resulting fragments will not disrupt the subdomain structure of the protein, 2) the catalytic and cofactor binding sites should all be contained in one fragment, and 3) resulting new N- and C-termini should be on the same face of the protein to avoid the need for long peptide linkers and allow for studies of orientation-dependence of protein binding.

It should be understood that the above mentioned criteria do not all need to be satisfied for a proper working of the present invention. It is an advantage that the enzyme

be small, preferably between 10-40 kDa. Although monomeric enzymes are preferred, multimeric enzymes can also be envisaged as within the scope of the present invention. The dimeric protein tyrosinase can be used in the instant assay. The information on the structure of the enzyme provides an additional advantage in designing the PCA, but is not necessary. Indeed, an additional strategy, to develop PCAs is presented, based on a combination of exonuclease digestion-generated protein fragments followed by directed protein evolution in application to the enzyme aminoglycoside kinase. Although the overexpression in prokaryotic cells is preferred it is not a necessity. It will be understood to the skilled artisan that the enzyme catalytic site (of the chosen enzyme) does not absolutely need to be on same molecule.

The '964 patent explains the rationale and criteria for using a particular enzyme in a PCA. FIG. 1 shows a general description of a PCA. The gene for a protein or enzyme is rationally dissected into two or more fragments. Using molecular biology techniques, the chosen fragments are subcloned, and to the 5' ends of each, proteins that either are known or thought to interact are fused. Co-transfection or transformation these DNA constructs into cells is then carried out. Reassembly of the probe protein or enzyme from its fragments is catalyzed by the binding of the test proteins to each other, and reconstitution is observed with some assay. It is crucial to understand that these assays will only work if the fused, interacting proteins catalyze the reassembly of the enzyme. That is, observation of reconstituted enzyme activity must be a measure of the interaction of the fused proteins."

THE REJECTION UNDER 35 U.S.C. § 112 SECOND PARAGRAPH

Claims 1, 3-4, 18-19, and 21-33 stand rejected under 35 U.S.C. second paragraph. It is believed that the current claim amendments render this rejection moot and accordingly withdrawal of this rejection is respectfully requested.

THE REJECTION UNDER 35 U.S.C. § 102(b)

Claims 1, 3-4 and 18-19, 21-24, 31-32 stand rejected under 35 U.S.C. § 102 (b) as being anticipated by Pelletier et al (Protein Engineering, 1997, vol. 10, page 89). The Examiner states that the present application gets the priority date of provisional application 60/141,210 filing date 6/26/99.

This rejection is rendered moot as the Examiner has agreed as per the interview of July 15th, 2004, to grant priority back to Canadian 2196496 which is the priority document of US serial No. 09/017412 upon the filing of the new oath/declaration.

The Examiner further asserts that "Pelletier et al disclose a protein complementation assay for detection of protein-protein interaction in vivo. The reference discloses a protein complementation assay based on reconstitution of DHFR activity. The reference discloses that the direct assay disclosed requires no additional endogenous factors for detecting specific protein-protein interactions. The reference discloses that DHFR is used as reporter enzyme, and GCN4 leucine zippers as model interacting proteins because of their association is well characterized. The reference in figure 1 discloses that the fragments of reporter molecules interaction with leucine zipper proteins (refers to the panel of molecules of the instant claims). The reference discloses

that the method is useful in identifying protein-protein interactions. The reference specifically teaches that the method is applicable to screening cDNA libraries for the detection of unknown, specific protein-protein interactions. Thus, the reference clearly anticipates the claimed invention."

The exact language used by the Examiner in outlining the rejection appears in applicants priority document CA 2196496 a copy of which is enclosed. Note in particular page 32, line 21, wherein applicant specifically discloses that the protein complementation assay of the invention allow for screening of cDNA libraries for protein-protein interactions.

Withdrawal of the rejection is respectfully requested.

THE REJECTION UNDER 35 U.S.C. § 102(e)

Claims 1, 3-4 and 18-19 21-24, 31-32 stand rejected under 35 U.S.C. § 102 (e) as being anticipated by U.S. Patent 6,270,964 (Michnick, et al). The rejection of claims 1, 3-4 and 18-19 21-24, 31-32 is now moot since Applicants' claim C-I-P status from the application which matured into the '964 patent (granting priority to the Canadian application), there is also common inventorship (Michnick and Pelletier) as well as ***common ownership***. Accordingly the '964 publication can not be used against applicants.

DOUBLE PATENTING

Claims 1, 3-4, 18-19, 21-33 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-41 of U.S. Patent No. 6,270,964B1. The Examiner states that ... "Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference claims are drawn to a method of detecting biomolecular interactions, and the method steps are same as the instant claimed method. The reference enzyme reporter molecule (species) refers to the protein reporter molecules (genus); other molecules of the reference refer to the panel of molecules of the instant claims; and the reference method detects interaction between the enzyme fragment and other molecules, which would certainly would result in identifying the interacting set of molecules of the instant claims. Thus it would be obvious to one skill in the art to use the reference method to identify the interacting set of molecules."

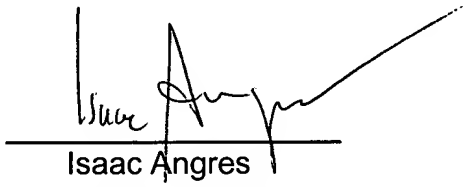
Upon receipt of a notice of allowable subject matter, Applicant will submit a terminal disclaimer.

This double patenting rejection confirms Applicants' position that there is full support for the priority date going back to USSN 09/017412 filed February 2, 1998 and claiming priority to Canada 2196496 filed January 31, 1997.

Regarding the draftsman requirement for corrections, Applicant will submit formal drawings after allowable subject matter is indicated.

In view of the above amendments and remarks, it is respectfully submitted that the claims are now in condition for allowance. Reconsideration and withdrawal of the rejections and objections are requested. The Examiner is invited to contact the undersigned at 703-418-2777 if he feels that further discussion may facilitate the resolution of any outstanding issues. An early indication of a Notice of Allowance is earnestly solicited.

Respectfully submitted,



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